

SUPPLEMENTAL MATERIAL

Title: Blood pressure effects of sodium reduction: a dose-response meta-analysis of experimental studies

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Table I. Search strategies for online databases.

Database	Search Strategy
PubMed/MEDLINE	((“blood pressure”[MH] OR “blood pressure determination”[MH] OR “arterial pressure”[MH] OR “hypertension”[MH] OR “blood pressure”[tiab] OR “hypertension”[tiab]) AND (“sodium, dietary”[MH] OR “sodium”[MH] OR “sodium chloride”[MH] OR “sodium”[tiab] OR “sodium chloride”[tiab]) AND (“randomized controlled trial”[Publication Type] OR “controlled clinical trial”[Publication Type] OR “randomized”[tiab] OR “placebo”[tiab] OR “randomly”[tiab] OR “trial”[tiab]) NOT (“animals”[MH] NOT “humans”[MH])) NOT("review"[Publication Type])
EMBASE	('sodium chloride'/exp OR 'sodium intake'/exp OR 'sodium restriction'/exp) AND ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp) AND 'human'/de AND 'article'/it NOT [medline]/lim
Cochrane CENTRAL	"sodium" in Record Title AND blood pressure in Title Abstract Keyword - in Trials (Word variations have been searched)

Table II. Summary of the trial interventions and achieved urinary sodium reduction.

Reference	Population	Sex	Hyp.	Anti-hyp. drug	Sodium reduction	Intervention	Achieved difference Na excretion	Intervention type
Alli 1992 ³⁴	26t-30c	both	yes	no	LSD (advice)	NSD (no advice)	+8	diet
Ames 2001 ³⁵ (Gr1) non diabetics (Gr2) diabetics	13 8	both	yes	yes	LSD (advice)+placebo	LSD (advice)+~136mmol/day	-133 -115	suppl.
Andersson 1984 ³⁶	10t-13c	men	yes	no	LSD (advice)+low energy	LSD (advice)+low energy+tables (8mmol each)	-99	suppl.
ANHMRC 1989a ³⁷	50t-53c	both	yes	no	LSD (advice ≤80mmol/day)+placebo	LSD (advice)+80mmol/day	-71	suppl.
ANHMRC 1989b ³⁸	44	both	yes	no	LSD (advice)+placebo	LSD (advice)+80mmol/day	-66	suppl.
Appel 2001 ³⁹	317t-296c	both (M+W)	yes	no	LSD (advice ≤80mmol/day)	NSD (no advice)	-40	diet
Arroll 1995 ⁴⁰ (Gr1) (Gr1)	44t-43c 48t-46c	both	yes	yes	LSD (advice) LSD (advice)+exercise	NSD (no advice) NSD (no advice)+exercise	+15 -16	diet
Beard 1982 ⁴¹	45t-45c	both	yes	yes	LSD (advice)	NSD (advice)	-99	diet
Benetos 1992 ⁴²	20	both	yes	no	LSD (60-90mmol/day)+placebo	LSD(60-90mmol/day)+~80mmol/day	-78	suppl.
Bulpitt 1984 ⁴³	32t-33c	both	yes	yes	LSD (advice 44 mmol/day decrease)+salt substitute	NSD (no advice)+salt substitute	-18	diet
Cappuccio 1997 ⁴⁴	47	Both	both (no+yes)	no	LSD (advice ≈80mmol/day)+placebo	LSD (≈80mmol/day)+120 mmol/day	-83	suppl.
Cappuccio 2006 ⁴⁵	399t-402c	both	both	yes	LSD (advice)+highK	NSD (advice)+highK	+5	diet
Carney 1991 ⁴⁶	11	both	yes	yes (w and w/o diuretics)	LSD (advice)+placebo	LSD (advice)+100 mmol/day	-102	suppl.
Chalmers 1986 ⁴⁷ (diet phase) (Gr1) (Gr2) (Gr3) (Gr4) (Gr5) (Gr6)	48t-52c 11t-9c 23t-20c 13t-11c 24t-23c 13t-14c 9t-10c	both	yes	no	LSD (advice) NSD (no advice)+placebo HighK diet+placebo LSD (advice)+placebo LSD (advice)+highK diet+placebo NSD (no advice)+highK 64mmol/day+placebo LSD (advice)+highK 64mmol/day+placebo	NSD (no advice) NSD (no advice)+80mmol/day HighK diet+80mmol/day LSD (advice)+80mmol/day LSD (advice)+highK diet+80mmol/day NSD (no advice)+highK 64mmol/day+80 mmol/day LSD (advice)+highK 64mmol/day+80mmol/day	-78 -36 -35 -54 -64 -82 -104	diet suppl.
Cobiac 1992 ⁴⁸ (Gr1) (Gr2)	26t-28c 25t-27c	both	no	-	LSD+sunflower oil+placebo LSD+fish oil+placebo	LSD+sunflower oil+80mmol/day LSD+fish oil+80mmol/day	-73 -68	suppl.
De Keyzer 2015 ⁴⁹	23	both	yes	yes	LSD (advice)	NSD (advice)	-28	diet
de Vries 2016 ⁵⁰	22	both	yes	yes	LSD ≈50mmol/day	NSD 150mmol/day	-77	diet
Dickinson 2014 ⁵¹	25	both	no	-	LSD (advice)	LSD + 60mmol/day	-42	suppl.

Dodson 1989 ⁵² (Ph1) (Ph2)	17t-17c 9	both	yes	yes	LSD (advice) LSD (advice)+placebo	NSD (no advice) LSD (advice)+80mmol/day	-59 -76	diet suppl.
Erwtelman 1984 ⁵³ (Ph1) (Ph2) (Ph3) (Ph4)	50t-44c	men	yes	no yes yes yes	LSD (advice)+placebo LSD (advice)+chlorthalidone LSD (advice)+metoprolol LSD (advice)+combination	NSD (advice)+placebo NSD (advice)+chlorthalidone NSD (advice)+metoprolol NSD (advice)+combination	-58 -55 -61 -58	diet
Fagerberg 1984 ⁵⁴	15t-15c	men	yes	no	LSD (advice)+low energy	LSD (advice)+low energy+tablets (8mmol/each)	-89	suppl.
Fagerberg 1985a ⁵⁵	10t-8c	men	yes	no	LSD (advice)+low energy	LSD (advice)+low energy+tablets (8mmol/each)	-110	suppl.
Fagerberg 1985b ⁵⁶	15t-15c	men	yes	no	LSD (advice)+low energy	LSD (advice)+low energy+tablets (8mmol/each)	-89	suppl.
Fotherby 1993 ⁵⁷	17	both	yes	no	LSD (advice 80-100mmol/day)+placebo	LSD (advice 80-100mmol/day)+80mmol/day	-79	suppl.
Gates 2004 ⁵⁸	12	both	yes	no	LSD (advice)+placebo	LSD (advice)+tablets (10mmol/day each)	-88	suppl.
Gijsbers 2015 ⁵⁹	36	both	yes	no	LSD (advice ≈100 mmol/day)+placebo	LSD (advice ≈100 mmol/day)+≈130mmol/day	-98	suppl.
Gillies 1984 ⁶⁰	24	both	yes	yes	LSD (advice)	NSD (no advice)	-77	diet
Grobbee 1987 ⁶¹	34	both	yes	yes	LSD (advice)+placebo	LSD (advice)+90mmol/day	-72	suppl.
He 2010 ⁶²	169	both	yes	no	LSD (advice ≈85mmol/day)+placebo	LSD (advice 85mmol/day)+90mmol/day	-55	suppl.
He 2015 ⁶³	271t-261c	both	no	-	LSD (advice)	NSD (no advice)	-50	diet
Howe 1994 ⁶⁴ (Gr1) (Gr2)	14t-14c 14t-14c	both	yes	yes	LSD (advice ≈70 mmol/day)+olive oil+placebo LSD (advice ≈70 mmol/day)+fish oil+placebo	LSD (advice ≈70mmol/day)+olive oil+80mmol/day LSD (advice ≈70mmol/day)+fish oil+80mmol/day	-58 -77	suppl.
HPTRG 1990 ⁶⁵	174t-177c	both	both	no	LSD (advice)	NSD (no advice)	-13	diet
Hwang 2014 ⁶⁶	119t-126c	both	yes	yes	LSD (intensive advice <100mmol/day)	LSD (conventional advice)	-27	diet
Jablonski 2013 ⁶⁷	17	both	yes	yes	LSD (advice ≈50mmol/day)+placebo	LSD (advice ≈50mmol/day)+100mmol/day	-80	suppl.
James 1994 ⁶⁸	19	both	yes	no	LSD (advice <40mmol/day)	HSD (advice >225mmol/day)	-309	diet
James 1996 ⁶⁹ Men Women	24 8	men women	yes	no	LSD (advice <40mmol/day)	HSD (advice >225mmol/day)	-302 -258	diet
Jula 1994 ⁷⁰	38t-38c	both	yes	no	LSD (advice ≤70mmol/day)	NSD (advice)	-71	diet
Kwakernaak 2014 ⁷¹ (Ph1) (Ph2)	45	both	yes	yes (ACEi) yes (ACRI+HCT)	LSD (advice ≈50mmol/day)	NSD (advice ≈200mmol/day)	-76 -60	diet
Lee 2018 ⁷²	30t-28c	both	yes	no	LSD (advice)	NSD (advice)	+7	diet
MacGregor 1982 ⁷³	19	both	yes	no	LSD (advice 60-80mmol/day)+placebo	LSD (advice 60-80mmol/day)+90mmol/day	-76	suppl.
MacGregor 1987 ⁷⁴	15	both	yes	yes	LSD (advice ≈80mmol/day)+placebo	LSD (advice ≈80mmol/day)+100mmol/day	-100	suppl.
MacGregor 1989 ⁷⁵	20	both	yes	no	LSD (advice 30-50mmol/day)+placebo	LSD (advice 30-50mmol/day)+70mmol/day LSD(advice 30-50mmol/day)+170mmol/day	-59 -82	suppl.
Mascioli 1991 ⁷⁶ (Gr1) sodium first (Gr2) placebo first	25	both	no	-	LSD (advice ≤35mmol/day)+placebo	LSD (advice ≤35mmol/day)+100mmol/day	-42 -80	suppl.

Maxwell 1984 ⁷⁷	18t-12c	both	yes	no	LSD (advice ≈40mmol/day)	LSD (advice ≈40mmol/day)+tables up to 210mmol/day	-171	suppl.
McCarron 1997 ⁷⁸	99	both	yes	yes	LSD (advice 60-80mmol/day)+placebo	LSD (advice 60-80mmol/day)+100mmol/day	-55	suppl.
Meland 1997 ⁷⁹	16	both	yes	no	LSD (advice)+placebo	LSD (advice)+50mmol/day	-66	suppl.
Meland 2009 ⁸⁰	23	both	yes	yes	LSD (advice)+placebo	LSD (advice)+50mmol/day	-38	suppl.
Melander 2007 ⁸¹ (Gr1) (Gr2)	21 18	both	yes no	no	LSD (advice 50mmol/day)+placebo	LSD (advice 50mmol/day)+100mmol/day	-93 -85	suppl.
Morgan 1981 ⁸² (Gr1) (Gr2)	6t-6c 6t-6c	men women	yes	yes	LSD (advice 70mmol/day)	NSD (no advice)	-98 -78	diet
Morgan 1987 ⁸³	10t-10c	men	yes	yes	LSD (advice 50-75mmol/day)	NSD (no advice)	-85	diet
Muhlhauser 1996 ⁸⁴	8t-8c	both	yes	no	LSD (advice ≈90mmol/day)+placebo	LSD (advice ≈90mmol/day)+100mmol/day	-95	suppl.
Nakano 2016 ⁸⁵	51t-44c	both	yes	yes	LSD (advice ≈100 mmol/day))	NSD (advice)	-39	diet
Nestel 1993 ⁸⁶ (Gr1) (Gr2)	17t-19c 15t-15c	men women	no	-	LSD (advice ≈80mmol/day)+placebo LSD (advice ≈70mmol/day)+placebo	LSD (advice ≈80mmol/day)+80mmol/day LSD (advice ≈70mmol/day)+80mmol/day	-76 -94	suppl.
Nowson 1988 ⁸⁷ (Gr1) (Gr2)	52t-55c 53t-52c	both	yes	no	LSD (advice 50-70mmol/day) LSD (advice 50-70mmol/day)+high K	NSD (no advice) NSD (no advice)+high K	-70 -72	diet
Nowson 2003 ⁸⁸	108	both	both	both (and no)	LSD (advice 50-70mmol/day)+placebo	LSD (advice 50-70mmol/day)+120mmol/day	-89	suppl.
Nowson 2009 ⁸⁹	46t-49c	women	both	both (no+yes)	LSD (advice DASH modified 'vitality diet')	NSD (advice 'reference healthy diet')	-42	diet
Parijs 1973 ⁹⁰ (Gr1) (Gr2)	18 18	both	Yes	no yes	LSD (advice)	NSD (advice)	-98 -62	diet
Parker 1990 ⁹¹ (Gr1) (Gr2)	15t-13c 16t-15c	men	yes	yes	LSD (advice <60mmol/day)+normal alcohol+placebo LSD (advice <60mmol/day)+low alcohol+placebo	LSD (advice <60mmol/day)+normal alcohol+100mmol/day LSD (advice <60mmol/day)+low alcohol+100mmol/day	-60 -83	suppl.
Parvanova 2018 ⁹²	57t-58c	both	yes	yes	LSD (advice ≈100mmol/day)	HSD (advice ≈200 mmol/day)	-44	diet
Pinjuh Markota 2015 ⁹³	76t-74c	both	yes	no	LSD (leaflet) with stickers	LSD (leaflet) w/o stickers	-28	diet
Puska 1983 ⁹⁴	34t-38c	both	both	no	LSD (advice)	NSD (no advice)	-117	diet
Redon-Mas 1993 ⁹⁵	235t-183c	both	yes	yes	LSD (advice <120mmol/day)	NSD (advice >120mmol/day, and >60 from run-in LSD phase)	-109	diet
Resnick 1994 ⁹⁶ (Gr1) Salt-sensitive (Gr2) Salt-insensitive	9 10	both	yes	both (no+yes)	LSD (advice <50mmol/day)	HSD (advice >200mmol/day)	-278 -253	diet
Richards 1984 ⁹⁷	12	both	yes	no	LSD (advice 80mmol/day)	LSD (advice 80mmol/day)+tablets up to 180mmol/day	-105	suppl.

Ruppert 1993 ⁹⁸	25	both	no	-	LSD (advice 85mmol/day)+placebo	LSD (advice 85mmol/day)+tablets up to 200mmol/day	-118	suppl.
Sacks 2001 ⁹⁹ (Gr1) (Gr2)	198 192	both	both	no	LSD (DASH) 50mmol/day LSD (CD) 50mmol/day	NSD (DASH) 100mmol/day/HSD (DASH) 150 mmol/day NSD (CD) 100mmol/day/HSD (CD) 150 mmol/day	-40/-37 -42/-35	diet
Schorr 1996 ¹⁰⁰ (Gr1) (Gr2)	16	both	no	-	LSD (advice <100mmol/day)+placebo	LSD+100mmol/day NaCl LSD+100mmol/day NaCO3	-71 -20	suppl.
Sciarrone 1992 ¹⁰¹	44t42c	both	yes	yes	LSD (advice<60mmol/day)+placebo	LSD (advice<60mmol/day)+100mmol/day	-89	suppl.
Silman 1983 ¹⁰²	12t-15c	both	yes	no	LSD (advice ≈100mmol/day)	NSD (advice)	-47	diet
Singer 1991 ¹⁰³	21	both	yes	yes	LSD (advice 80-100mol/day)+placebo	LSD (advice 80-100mol/day)+100mmol/day	-91	suppl.
Slagman 2011 ¹⁰⁴	52	both	yes	yes (ACEi) yes (ACE+ARB)	LSD (advice ≈50mmol/day)	NSD (advice ≈200mmol/day)	-83 -75	diet
Suckling 2016 ¹⁰⁵	46	both	yes	no	LSD (advice ≈90mml/day)+placebo	LSD (Advice ≈90mmol/day)+90mmol/day	-48	suppl.
Svetkey 2009 ¹⁰⁶ (Gr1) GP involved (Gr2) GP not involved	124t-122c 128t-134c	both	yes	yes	LSD (advice)	NSD (no advice)	-16 -23	diet
Swift 2005 ¹⁰⁷	40	both	yes	no	LSD (advice=90mmol/day)+placebo	LSD (advice ≈90mmol/day)+120mmol/day	-78	suppl.
Takahashi 2006 ¹⁰⁸	119t-116c	both	both	both	LSD (advice <170mmol/day in men and <135mmol/day in women)	NSD (no advice)	-38	diet
Todd 2012 ¹⁰⁹	23	both	no	-	LSD (advice <60mmol/day)+placebo in tomato juice	LSD (advice <60mmol/day)+90mmol/day in tomato juice LSD (advice <60mmol/day)+190mmol/day in tomato juice	-89 -47	suppl.
TOHP 1992 ¹¹⁰	327t-417c	both	no	-	LSD (advice)	NSD (no advice)	-44	diet
TOHP 1997 ¹¹¹ (Gr1) (Gr2)	515t-514c 537t-527c	both	no	-	LSD (advice <70mmol/day) LSD (advice <70mmol/day)+weight loss (4.5kg)	NSD (no advice) NSD (no advice)+weight loss (4.5kg)	-40 -25	diet
van Berge-Landry 2004 ¹¹²	48	both	yes	no	LSD (advice <40mmol/day)	HSD (advice >225mmol/day)	-285	diet
Vogt 2008 ¹¹³ (Ph1) (Ph2) (Ph3)	33	both	yes	no yes yes	LSD (advice ≈50mmol/day)+placebo LSD (advice ≈50mmol/day)+losartan LSD (advice ≈50mmol/day)+losartan+HCT	HSD (advice ≈200mmol/day)+placebo HSD (advice ≈200mmol/day)+losartan HSD (advice ≈200mmol/day)+losartan+HCT	-110 -105 -100	diet
Watt 1983 ¹¹⁴	18	both	yes	no	LSD (advice)+placebo	LSD (advice)+80mmol/day	-56	suppl.
Watt 1985 ¹¹⁵ (Gr1) both parents high BP (Gr2) both parents low BP	31 35	both	no	-	LSD (advice)+placebo	LSD (advice)+80mmol/day	-60 -74	suppl.
Weir 2010 ¹¹⁶	115	both	yes	yes	LSD (advice ≤100mmol/day)	HSD (advice ≥200mmol/day)	-123	diet

Wing 1998 ¹¹⁷ (Gr1) (Gr2)	17 17	both	yes	no yes	LSD (advice <100mol/day)+placebo LSD (advice <100mol/day)+placebo+indapamide	LSD (advice <100mmol/day)+80mmol/day LSD (advice <100mmol/day)+80mmol/day+indampamide	-59 -53	suppl.
Yamamoto 1997 ¹¹⁸	18t-18c	both	yes	yes	LSD (advice)	NSD (no advice)	-32	diet

Note: 'Advice' for sodium reduction were dietary recommendations ranging from instructions not to add salt during cooking and at the table, suggestion of dietary regimens, tailored diets prepared by a dietitian for study subjects, to more complex and sophisticated interventions including individual and/or group counselling for several weeks in order to assist participants in achieving and maintaining the desired interventions. Abbreviations: LSD: low sodium diet; NSD: normal sodium diet; HSD: high sodium diet; HCT: hydrochlorothiazide.

Table III. Risk of bias (RoB) of included studies. Domains are (1) randomization process errors; (2) deviations from the intended interventions; (3) missing outcome data; (4) measurement of the outcome; (5) selection of the reported result.

Reference	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall RoB
Alli 1992 ³⁴	Some concerns	High	Low	Low	Some concerns	High
Ames 2001 ³⁵	Some concerns	Low	Low	Low	Low	Intermediate
Andersson 1984 ³⁶	Some concerns	Low	Low	Low	Low	Intermediate
ANHMRC 1989a ³⁷	Some concerns	Low	Low	Low	Low	Intermediate
ANHMRC 1989b ³⁸	Some concerns	Low	Low	Low	Low	Intermediate
Appel 2001 ³⁹	Some concerns	Low	Low	Low	Low	Intermediate
Arroll 1995 ⁴⁰	Some concerns	Low	Low	Low	Some concerns	Intermediate
Beard 1982 ⁴¹	Some concerns	Low	Low	Low	Some concerns	Intermediate
Benetos 1992 ⁴²	Some concerns	Low	Low	Low	Low	Intermediate
Bulpitt 1984 ⁴³	Some concerns	Low	Low	Low	Some concerns	Intermediate
Cappuccio 1997 ⁴⁴	Low	Low	Low	Low	Low	Low
Cappuccio 2006 ⁴⁵	Low	Low	Low	Some concerns	Low	Intermediate
Carney 1991 ⁴⁶	Low	Low	Low	Low	Low	Low
Chalmers 1986 ⁴⁷	Some concerns	Low	Low	Low	Low	Intermediate
Cobiac 1992 ⁴⁸	Some concerns	Low	Low	Low	Some concerns	Intermediate
De Keyzer 2015 ⁴⁹	High	Low	Low	Low	Low	High
de Vries 2016 ⁵⁰	Low	Low	Low	Low	Low	Low
Dickinson 2014 ⁵¹	Low	Low	Low	Low	Low	Low
Dodson 1989 ⁵² (parallel)	Some concerns	Low	Low	Low	Some concerns	Intermediate
Dodson 1989 ⁵² (crossover)	Some concerns	Low	Low	Low	Low	Intermediate
Erwtaman 1984 ⁵³	Some concerns	Low	Low	Low	Some concerns	Intermediate
Fagerberg 1984 ⁵⁴	Some concerns	Low	Low	Low	Some concerns	Intermediate
Fagerberg 1985a ⁵⁵	Some concerns	Low	Low	Low	Some concerns	Intermediate
Fagerberg 1985b ⁵⁶	Some concerns	Low	Low	Low	Some concerns	Intermediate
Fotherby 1993 ⁵⁷	Some concerns	Low	Low	Low	Low	Intermediate
Gates 2004 ⁵⁸	Some concerns	Low	Low	Low	Low	Intermediate
Gijsbers 2015 ⁵⁹	Some concerns	Low	Low	Low	Low	Intermediate
Gillies 1984 ⁶⁰	Some concerns	Low	Low	Low	Low	Intermediate
Grobbee 1987 ⁶¹	Some concerns	Low	Low	Low	Low	Intermediate
He 2010 ⁶²	Some concerns	Low	Low	Low	Low	Intermediate
He 2015 ⁶³	Low	Low	Low	Low	Low	Low
Howe 1994 ⁶⁴	Some concerns	Low	Low	Low	Some concerns	Intermediate
HPTRG 1990 ⁶⁵	Some concerns	Low	Low	Low	Low	Intermediate
Hwang 2014 ⁶⁶	Low	Low	Low	Low	Low	Low
Jablonski 2013 ⁶⁷	Some concerns	Low	Low	Low	Low	Intermediate
James 1994 ⁶⁸	Some concerns	Low	Low	Low	Low	Intermediate
James 1996 ⁶⁹	Some concerns	Low	Low	Low	Low	Intermediate
Jula 1994 ⁷⁰	Some concerns	Low	Low	Low	Low	Intermediate
Kwakernaak 2014 ⁷¹	Some concerns	Low	Low	Low	Low	Intermediate
Lee 2018 ⁷²	Some concerns	Low	Low	Low	Low	Intermediate
MacGregor 1982 ⁷³	Some concerns	Low	Low	Low	Low	Intermediate
MacGregor 1987 ⁷⁴	Some concerns	Low	Low	Low	Low	Intermediate
MacGregor 1989 ⁷⁵	Some concerns	Low	Low	Low	Low	Intermediate
Mascioli 1991 ⁷⁶	Some concerns	Low	Low	Low	Low	Intermediate
Maxwell 1984 ⁷⁷	Some concerns	Low	Low	Low	Some concerns	Intermediate
McCarron 1997 ⁷⁸	Some concerns	Low	Low	Low	Low	Intermediate
Meland 1997 ⁷⁹	Some concerns	Low	Low	Low	Low	Intermediate
Meland 2009 ⁸⁰	Some concerns	Low	Low	Low	Low	Intermediate
Melander 2007 ⁸¹	Some concerns	Low	Low	Low	Low	Intermediate
Morgan 1981 ⁸²	Some concerns	Low	Low	Low	Some concerns	Intermediate
Morgan 1987 ⁸³	Some concerns	Low	Low	Low	Some concerns	Intermediate
Muhlhauser 1996 ⁸⁴	Some concerns	Low	Low	Low	Low	Intermediate
Nakano 2016 ⁸⁵	Low	Low	Low	Low	Low	Low
Nestel 1993 ⁸⁶	Some concerns	Low	Low	Low	Some concerns	Intermediate
Nowson 1988 ⁸⁷	Some concerns	Low	Low	Low	Low	Intermediate
Nowson 2003 ⁸⁸	Some concerns	Low	Low	Low	Low	Intermediate
Nowson 2009 ⁸⁹	Some concerns	Low	Low	Low	Some concerns	Intermediate

Parijs 1973 ⁹⁰	Some concerns	Low	Low	Low	Low	Intermediate
Parker 1990 ⁹¹	Some concerns	Low	Low	Low	Some concerns	Intermediate
Parvanova 2018 ⁹²	Low	Low	Low	Low	Some concerns	Intermediate
Pinjuh Markota 2015 ⁹³	Low	Low	Low	Low	Some concerns	Intermediate
Puska 1983 ⁹⁴	Some concerns	Low	Low	Low	Low	Intermediate
Redon-Mas 1993 ⁹⁵	Some concerns	Low	Low	Low	Some concerns	Intermediate
Resnick 1994 ⁹⁶	Some concerns	Low	Low	Low	Low	Intermediate
Richards 1984 ⁹⁷	Some concerns	Low	Low	Low	Low	Intermediate
Ruppert 1993 ⁹⁸	Some concerns	Low	Low	Low	Low	Intermediate
Sacks 2001 ⁹⁹	Some concerns	Low	Low	Low	Low	Intermediate
Schorr 1996 ¹⁰⁰	Some concerns	Low	Low	Low	Low	Intermediate
Sciarrone 1992 ¹⁰¹	Some concerns	Low	Low	Low	Low	Intermediate
Silman 1983 ¹⁰²	Some concerns	Low	Low	Low	Low	Intermediate
Singer 1991 ¹⁰³	Some concerns	Low	Low	Low	Low	Intermediate
Slagman 2011 ¹⁰⁴	Low	Low	Low	Low	Low	Low
Suckling 2016 ¹⁰⁵	Some concerns	Low	Low	Low	Low	Intermediate
Svetkey 2009 ¹⁰⁶	Low	Low	Low	Low	Low	Low
Swift 2005 ¹⁰⁷	Some concerns	Low	Low	Low	Low	Intermediate
Takahashi 2006 ¹⁰⁸	Low	Low	Low	Low	Low	Low
Todd 2012 ¹⁰⁹	Some concerns	Low	Low	Low	Low	Intermediate
TOHP 1992 ¹¹⁰	Low	Low	Low	Low	Low	Low
TOHP 1997 ¹¹¹	Low	Low	Low	Low	Low	Low
van Berge-Landry 2004 ¹¹²	Some concerns	Low	Low	Low	Low	Intermediate
Vogt 2008 ¹¹³	Some concerns	Low	Low	Low	Low	Intermediate
Watt 1983 ¹¹⁴	Some concerns	Low	Low	Low	Low	Intermediate
Watt 1985 ¹¹⁵	Some concerns	Low	Low	Low	Low	Intermediate
Weir 2010 ¹¹⁶	Some concerns	Low	Low	Low	Low	Intermediate
Wing 1998 ¹¹⁷	Some concerns	Low	Low	Low	Low	Intermediate
Yamamoto 1997 ¹¹⁸	Some concerns	Low	Low	Low	Low	Intermediate

Figure I. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials divided by hypertension status (no hypertension and hypertension) and type of intervention (supplement and diet). The average curve (solid line) with 95% confidence limits (dashed lines) was estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

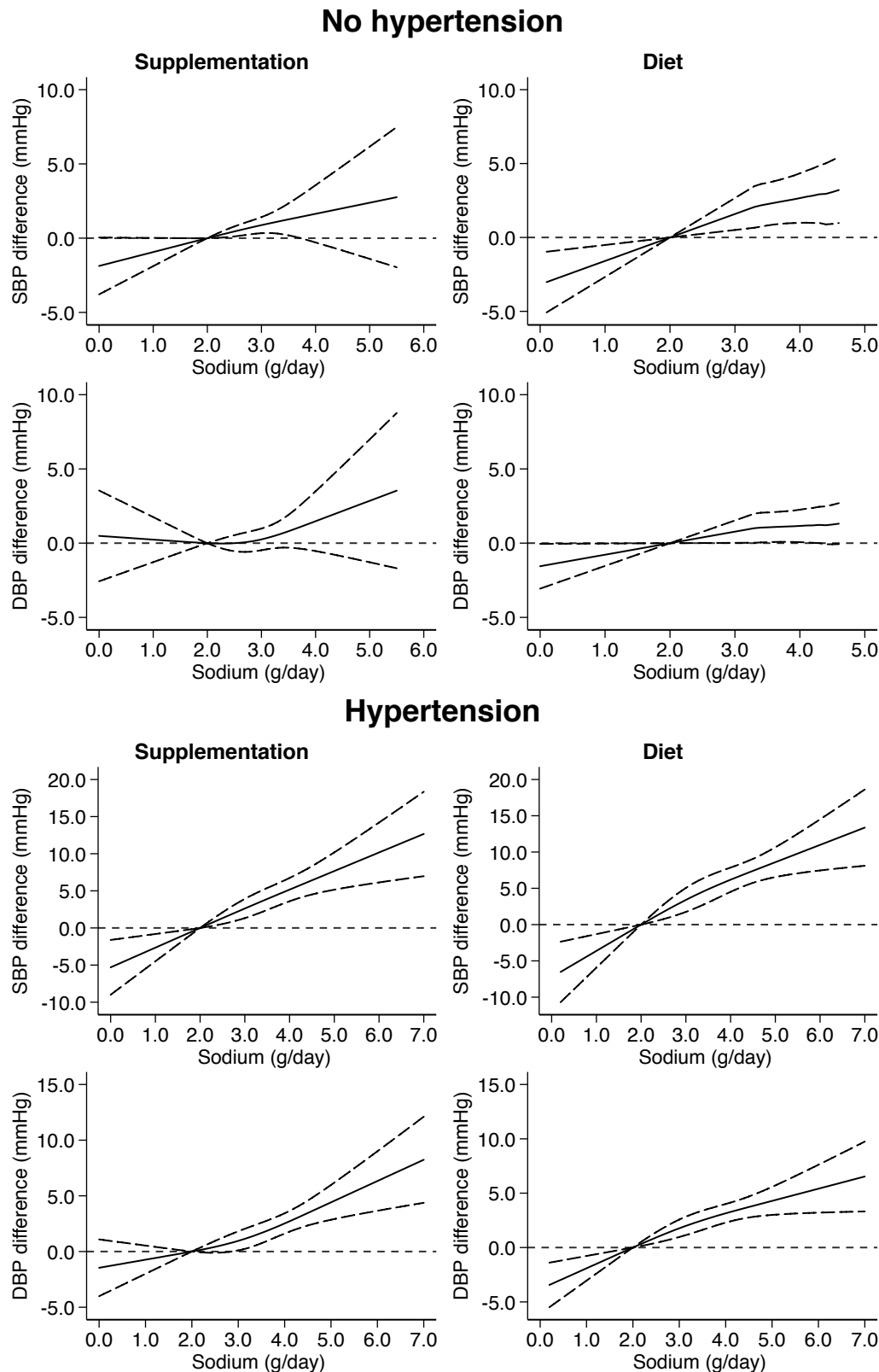


Figure II. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials in participants with hypertension divided by use of anti-hypertensive medication. The average curve (solid line) with 95% confidence limits (dashed lines) was estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

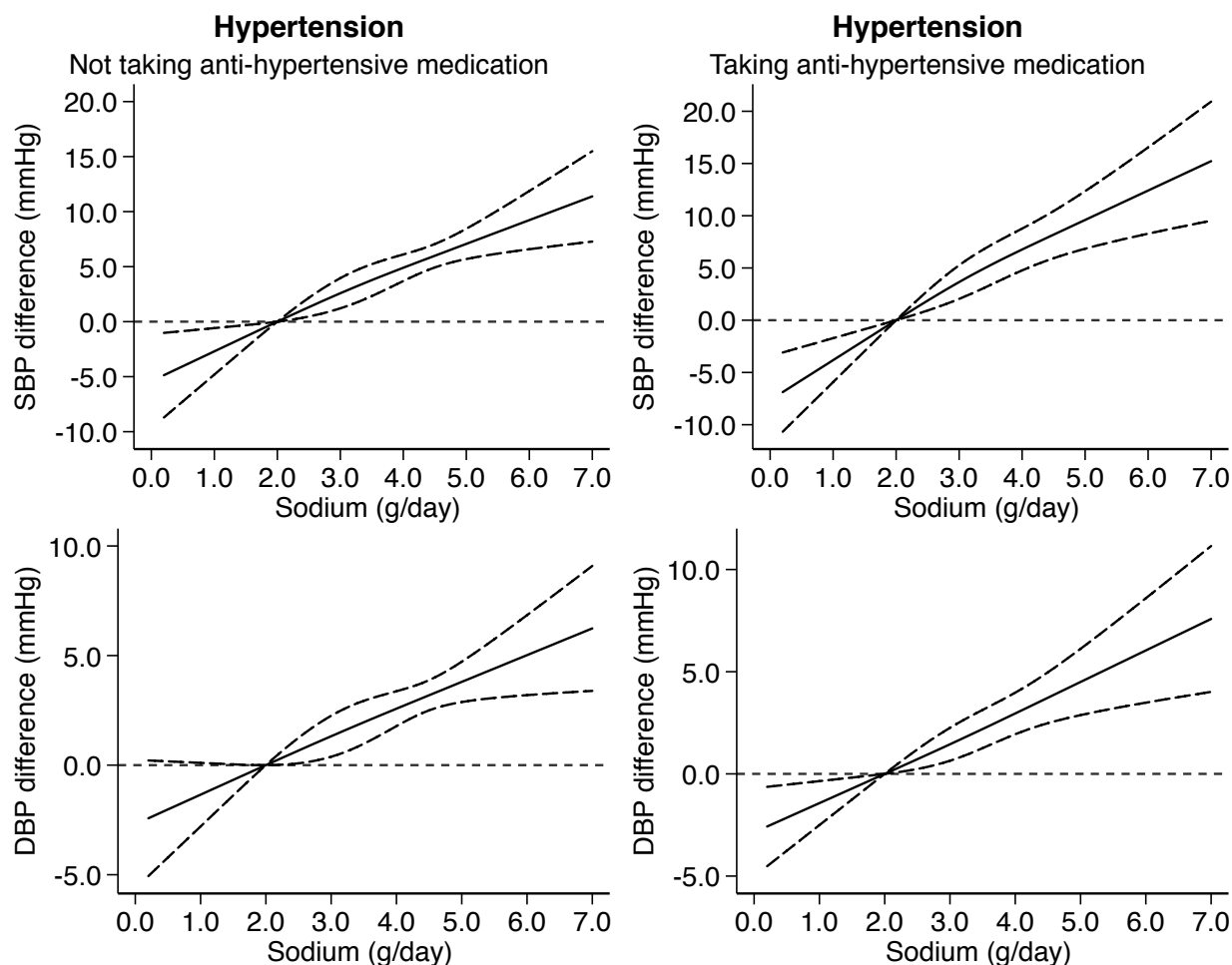


Figure III. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials in participants with hypertension taking anti-hypertensive medication divided by intervention type (supplement and diet). The average curve (solid line) with 95% confidence limits (dashed lines) was estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

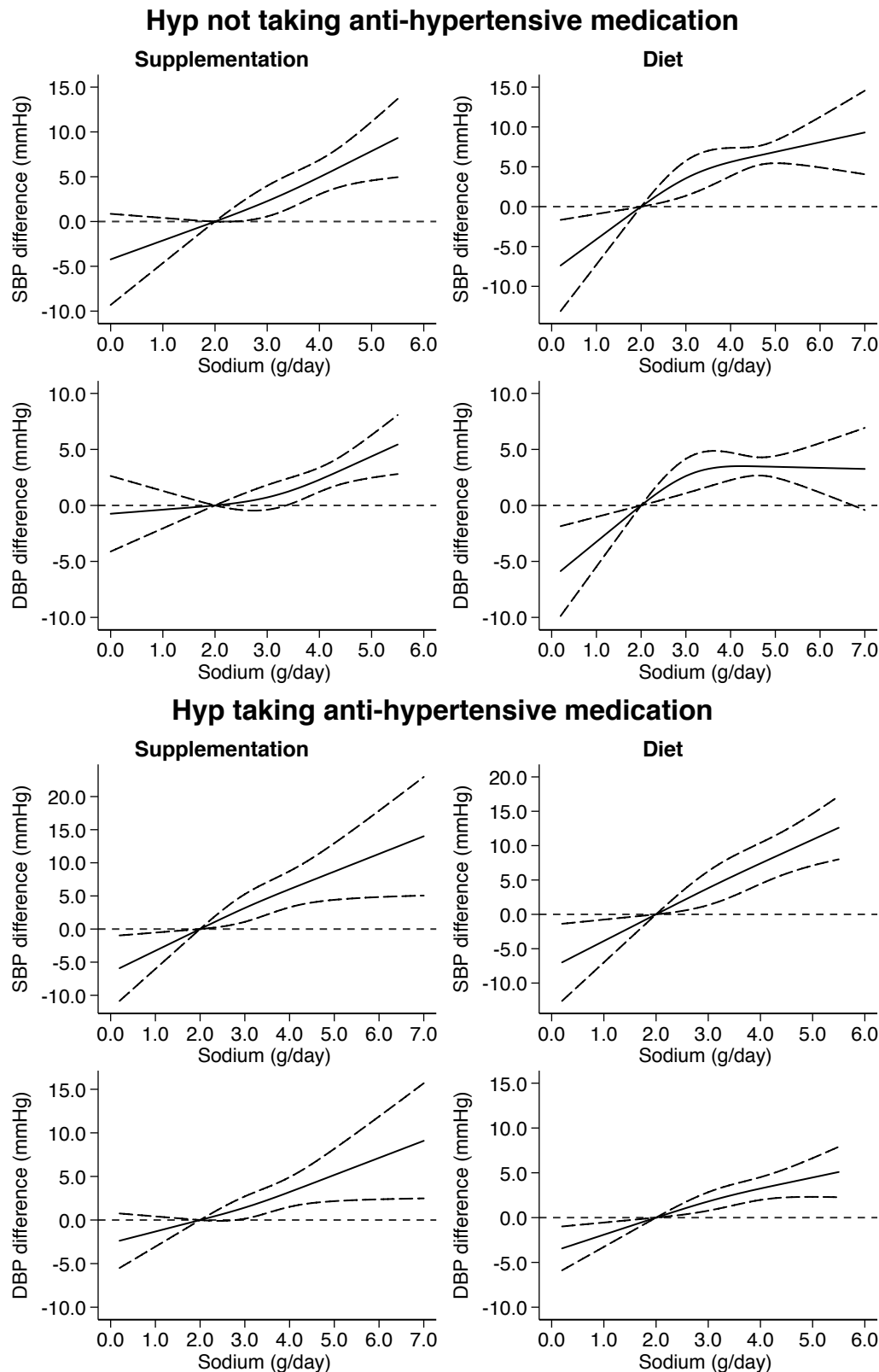


Figure IV. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials in participants with hypertension, stratified by baseline mean SBP levels (<140 mmHg versus ≥ 140 mmHg). Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

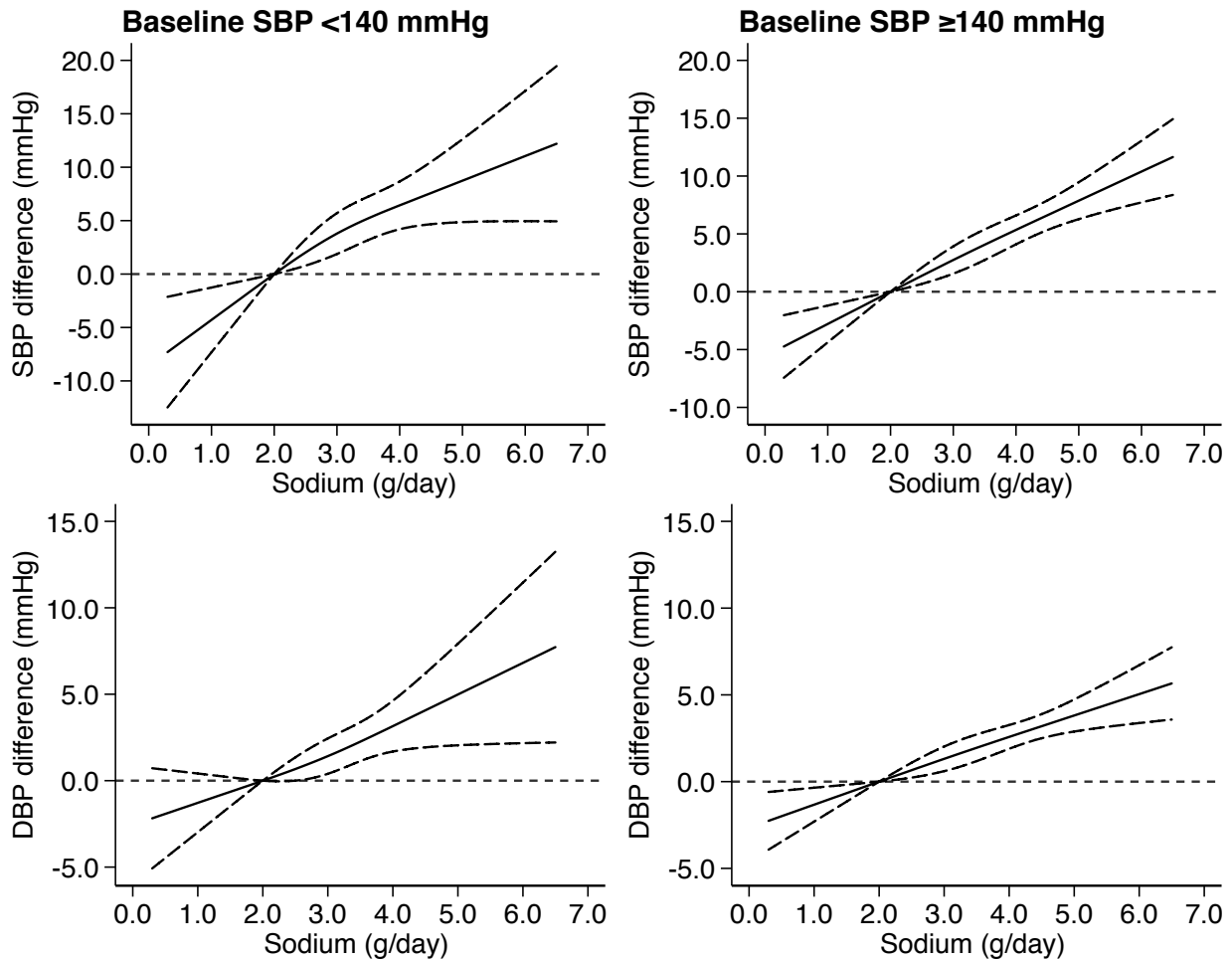


Figure V. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials in participants with hypertension not taking anti-hypertensive medications, stratified by baseline mean SBP levels (<140 mmHg versus \geq 140 mmHg). Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

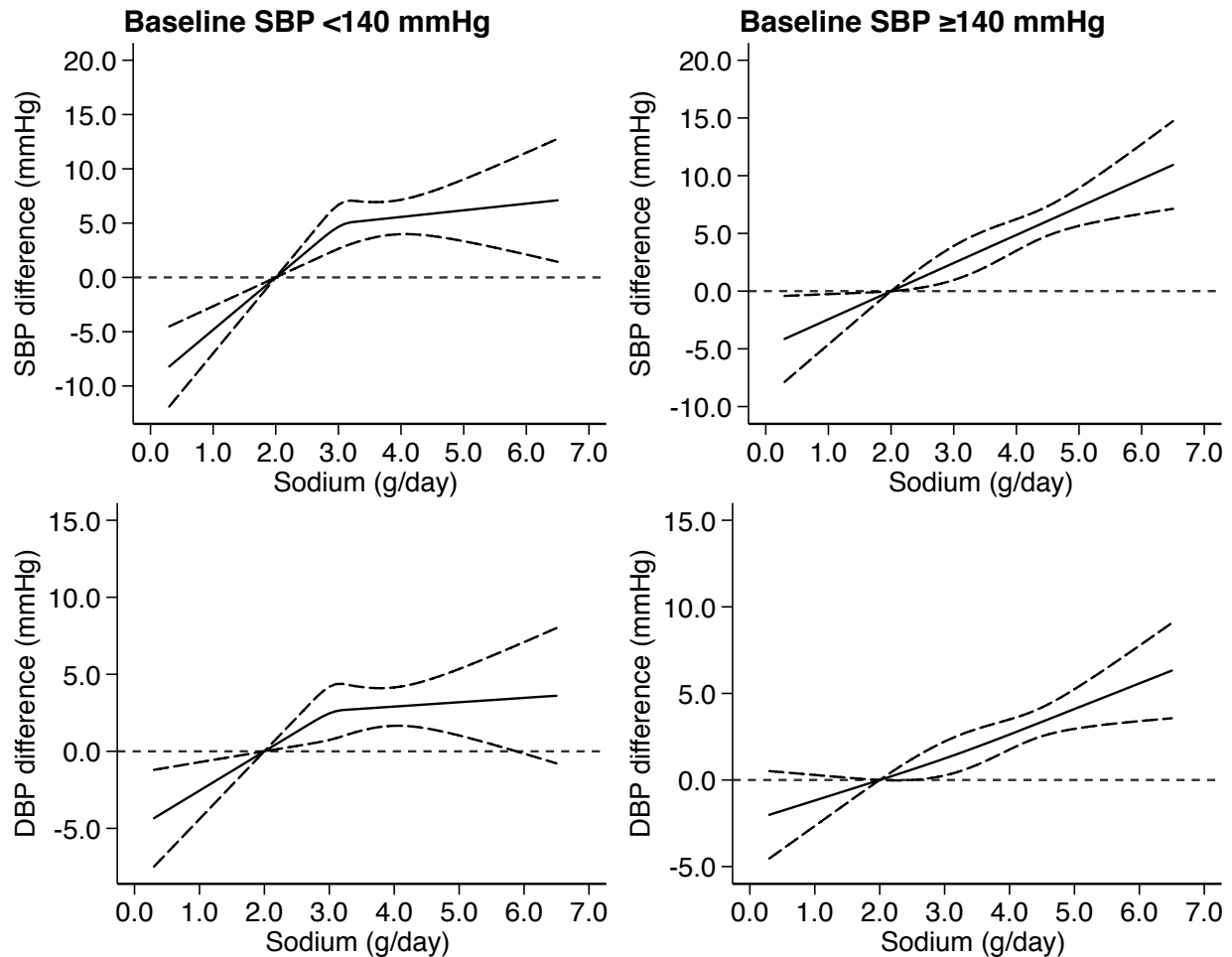


Figure VI. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials, stratifying by baseline sodium excretion (<109 mmol/day versus \geq 109 mmol/day, i.e. 2.5 g/day versus \geq 2.5 g/day). Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

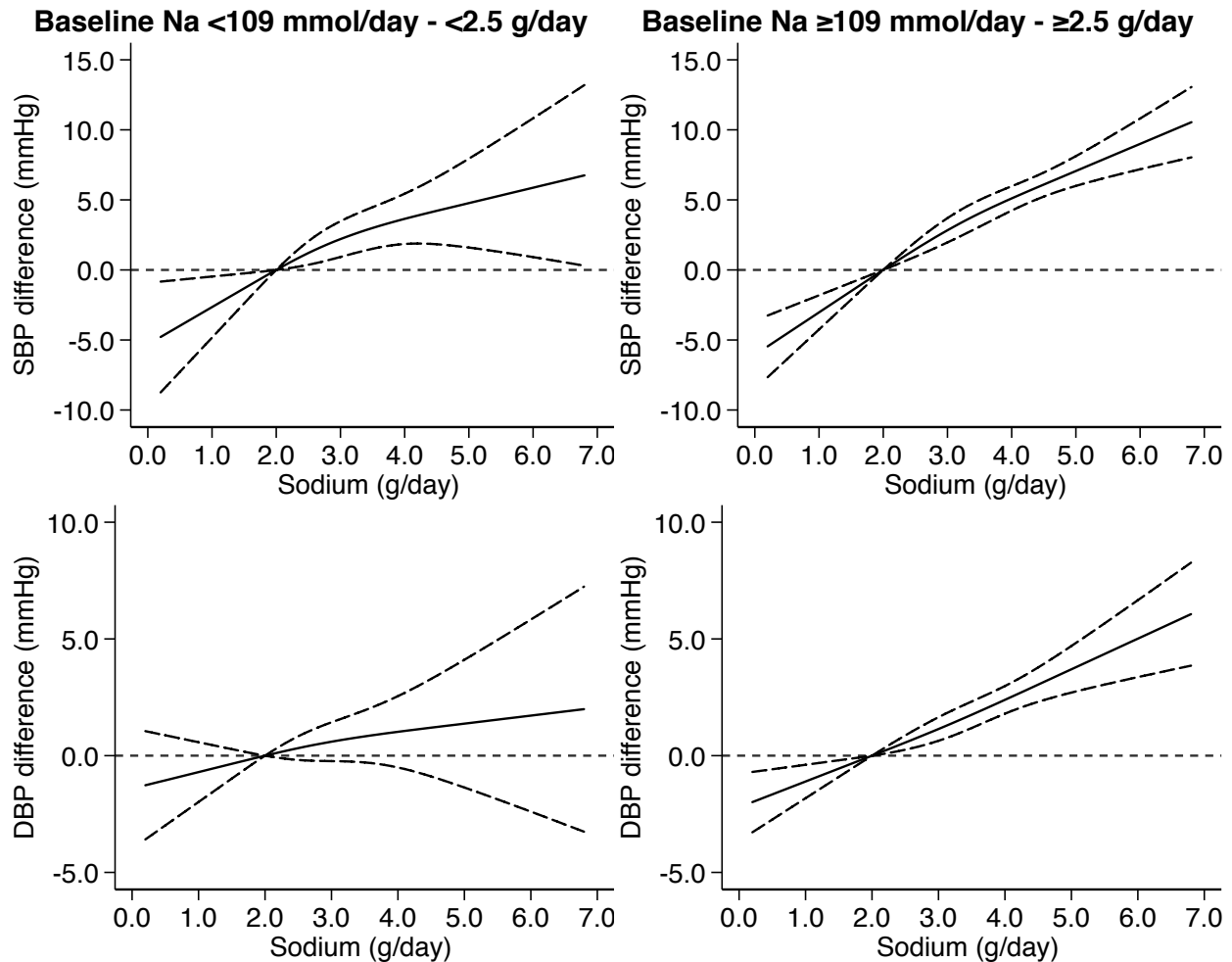


Figure VII. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials divided by hypertension status (no hypertension and hypertension) and trial duration (less or more/equal to 12 weeks). Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

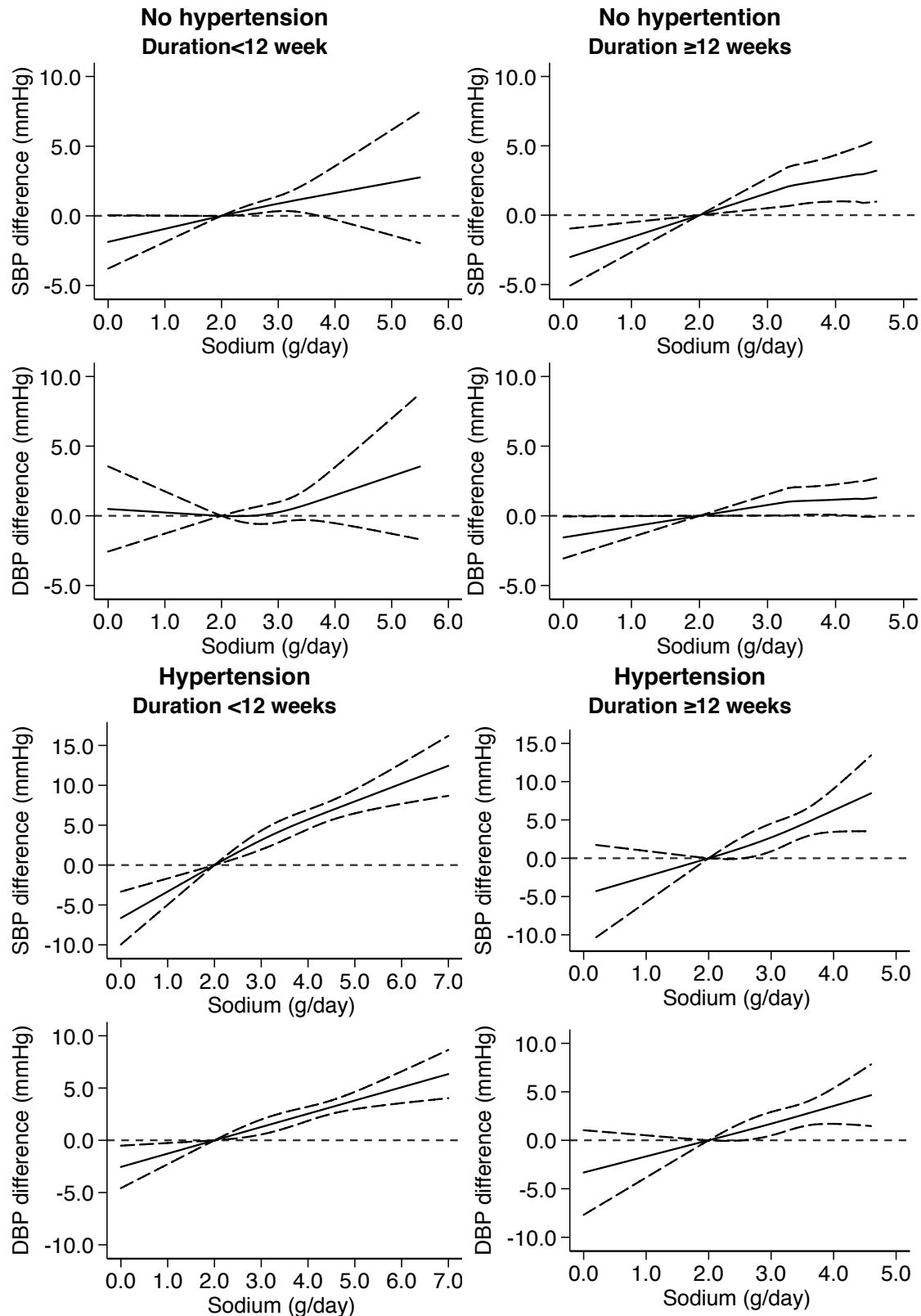


Figure VIII. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials stratified by study design (parallel or crossover arm design), also excluding crossover studies without a washout period. Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

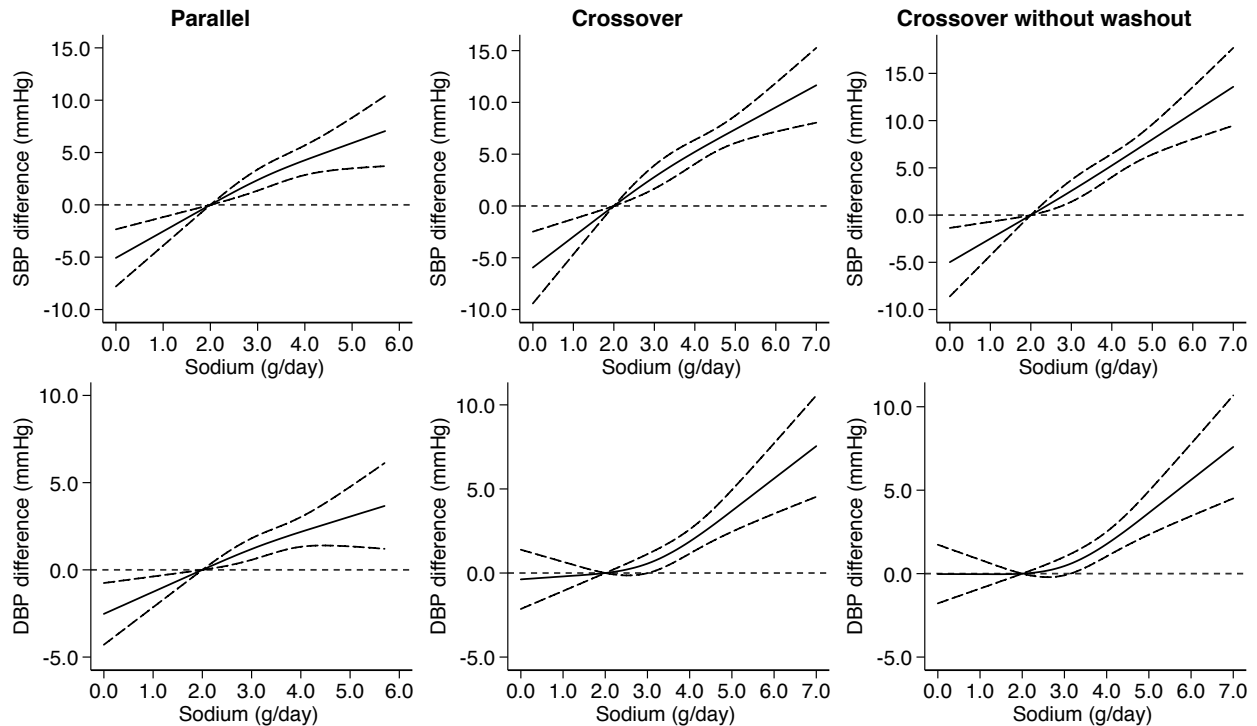


Figure IX. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials stratified by sex. Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

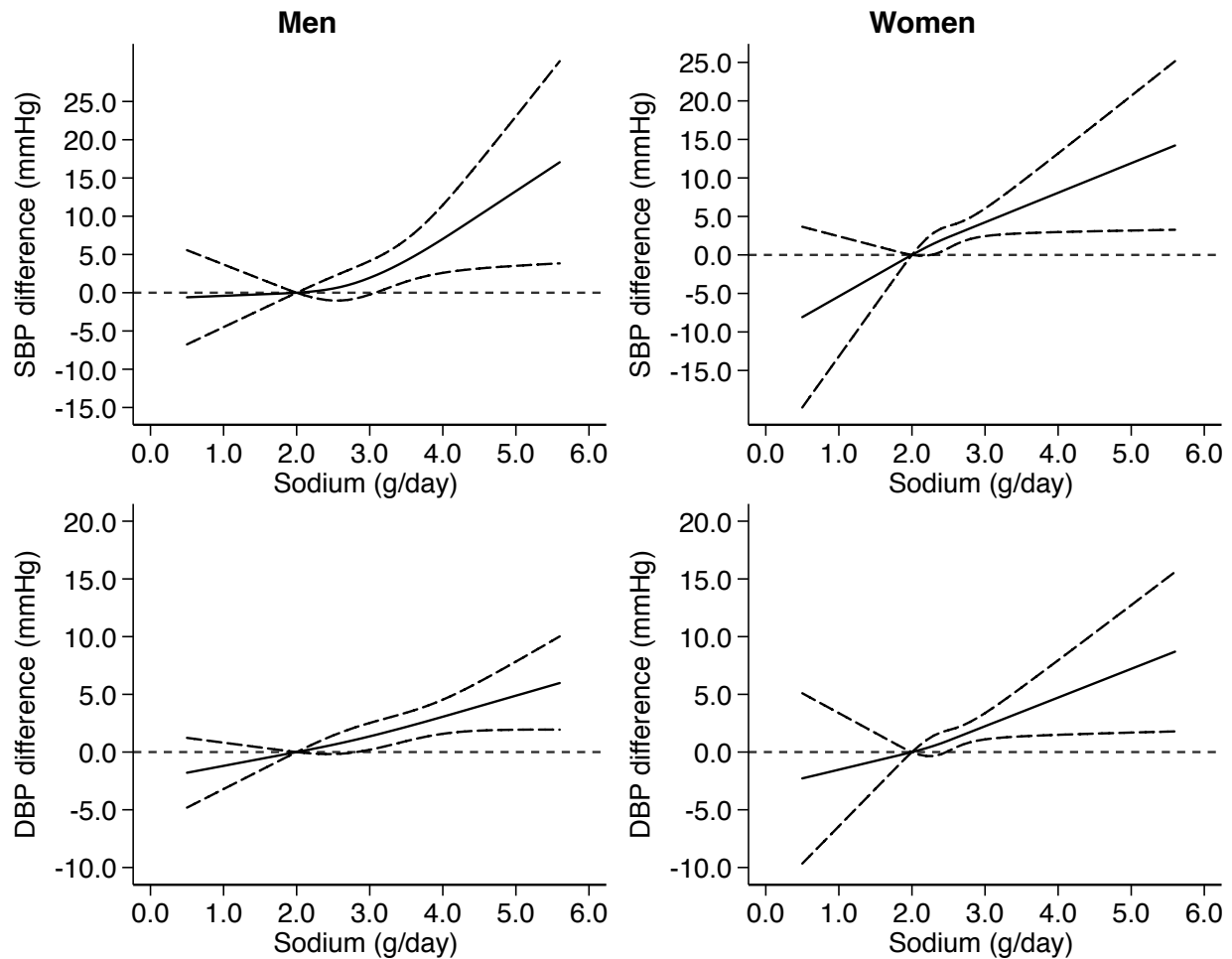


Figure X. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to the difference in sodium excretion in the treatment and control group at the end of the trials stratified by trial duration (less or more/equal to 12 weeks). Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model.

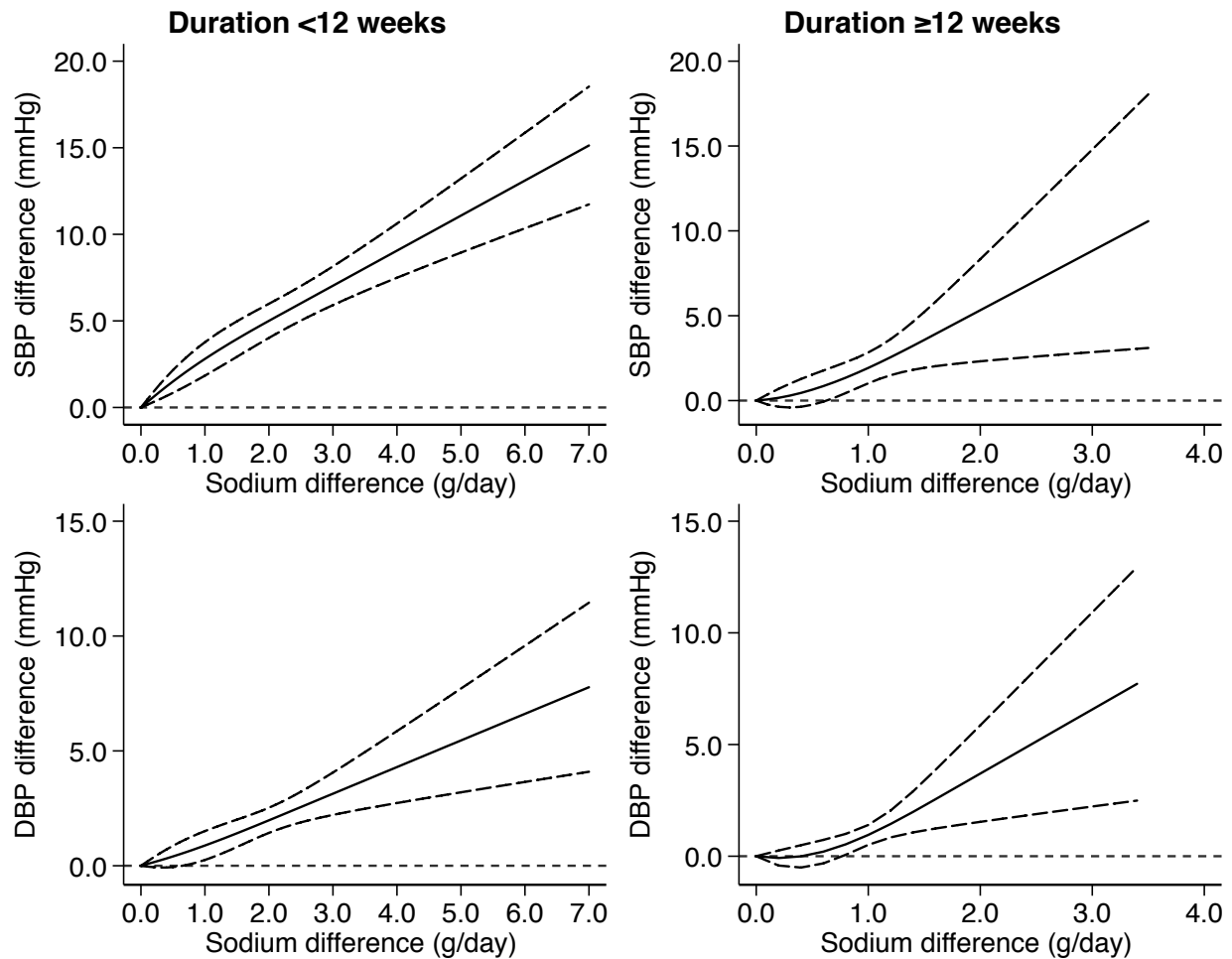


Figure XI. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mmHg) according to achieved sodium excretion in the treatment and control groups at the end of the trials (all studies), and by type of intervention (supplementation or diet), after excluding the two trials at high risk of bias. Average curve (solid line) with 95% confidence limits (dashed lines) estimated with a one-stage random-effects restricted cubic spline model, using 2 g/day as referent.

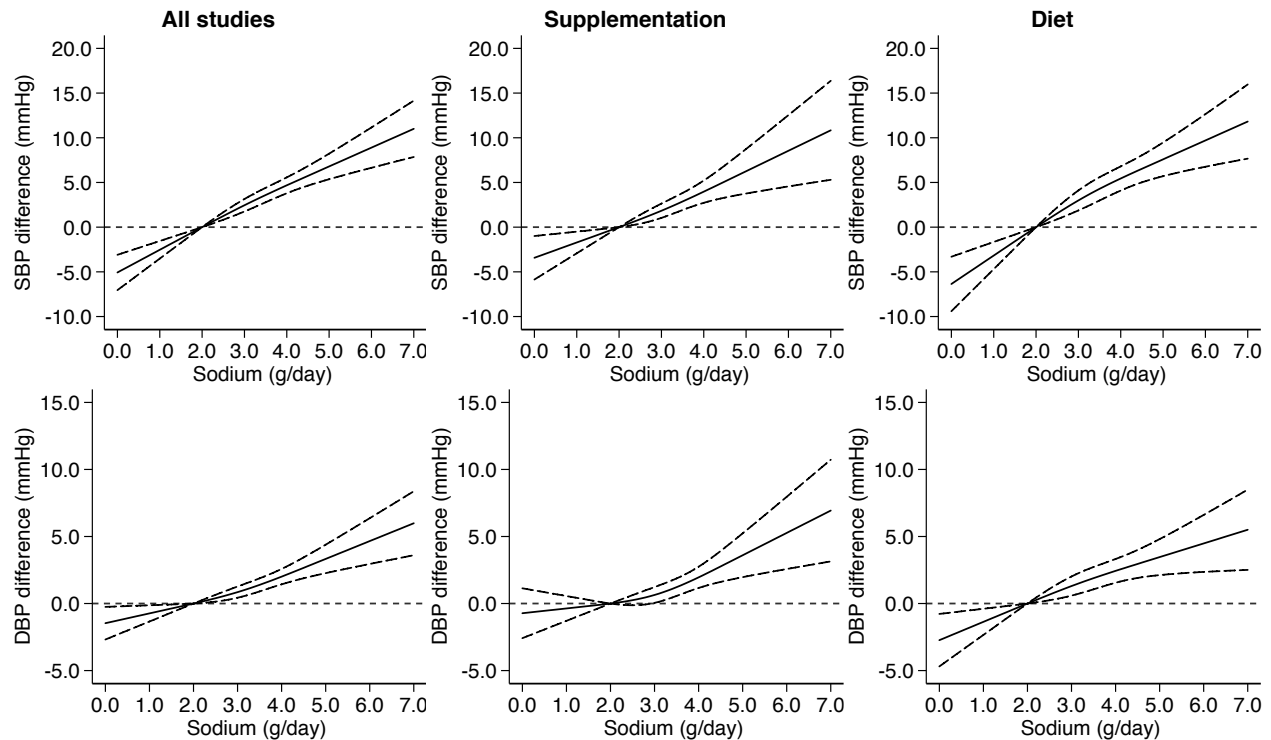


Figure XII. Funnel plots for mean difference (MD) of changes in systolic (SBP) and diastolic (DBP) blood pressure levels (as mmHg) and its standard error (SE).

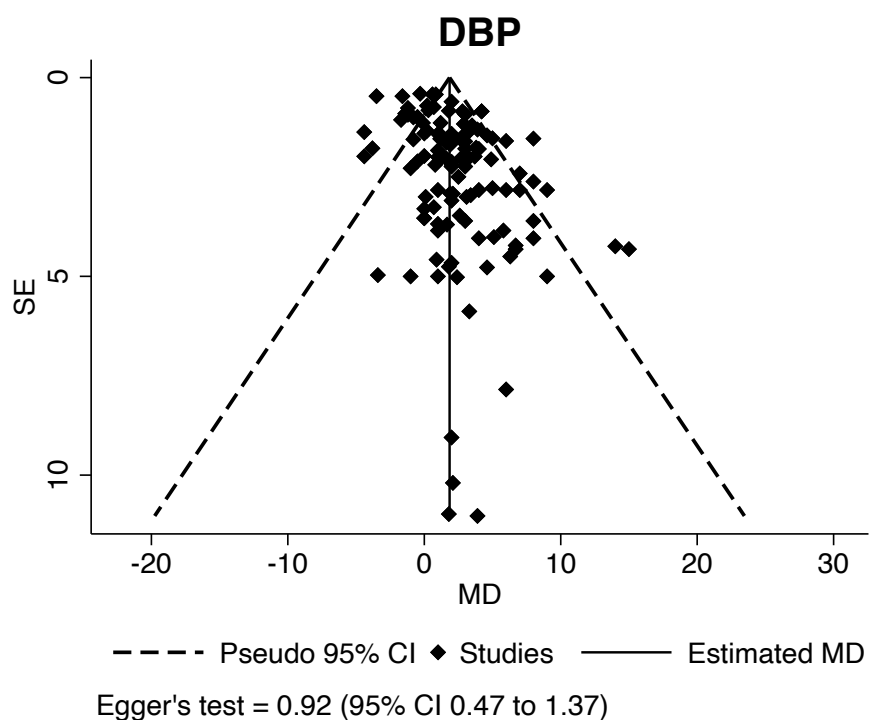
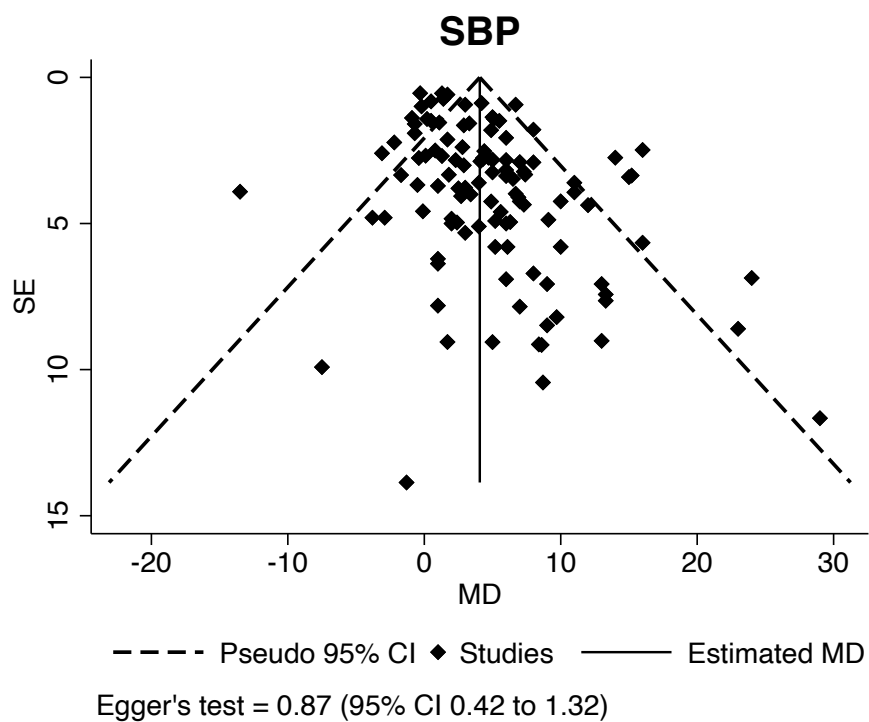


Figure XIII. Funnel plots for mean difference (MD) of changes in systolic (SBP) and diastolic (DBP) blood pressure levels (as mmHg) and its standard error (SE) using trim-and-fill method for small-study effects. Squared-diamonds indicate filled data.

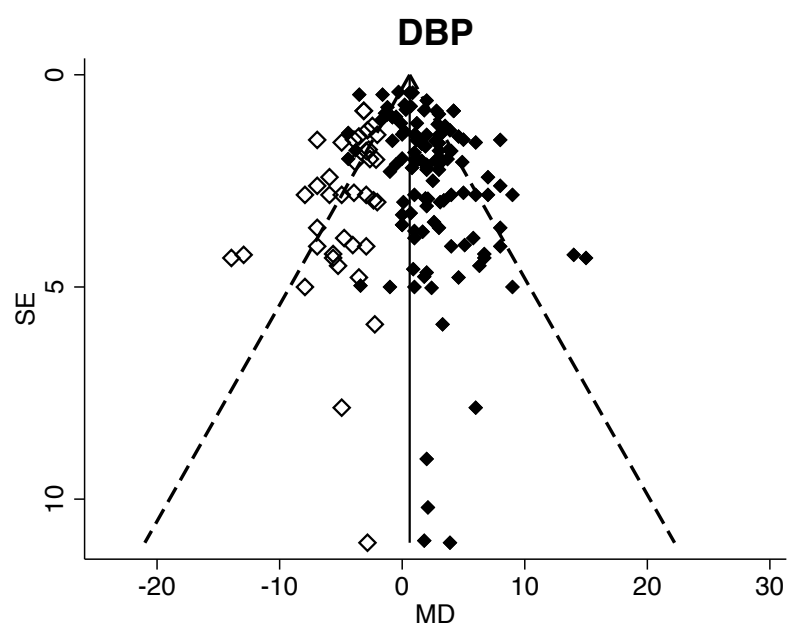
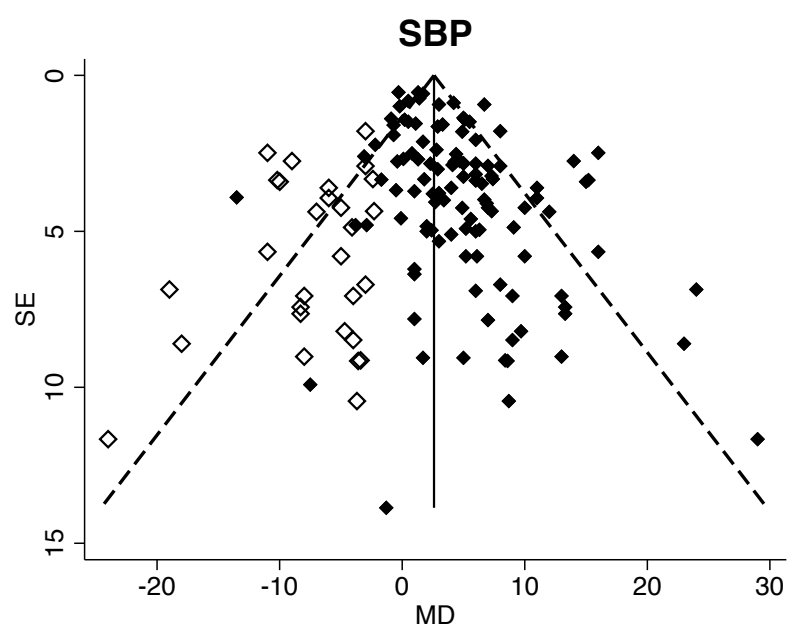


Figure XIV. Funnel plots for mean difference (MD) of changes in systolic (SBP) and diastolic (DBP) blood pressure levels (as mmHg) and its standard error (SE) divided by type of intervention (supplementation vs diet).

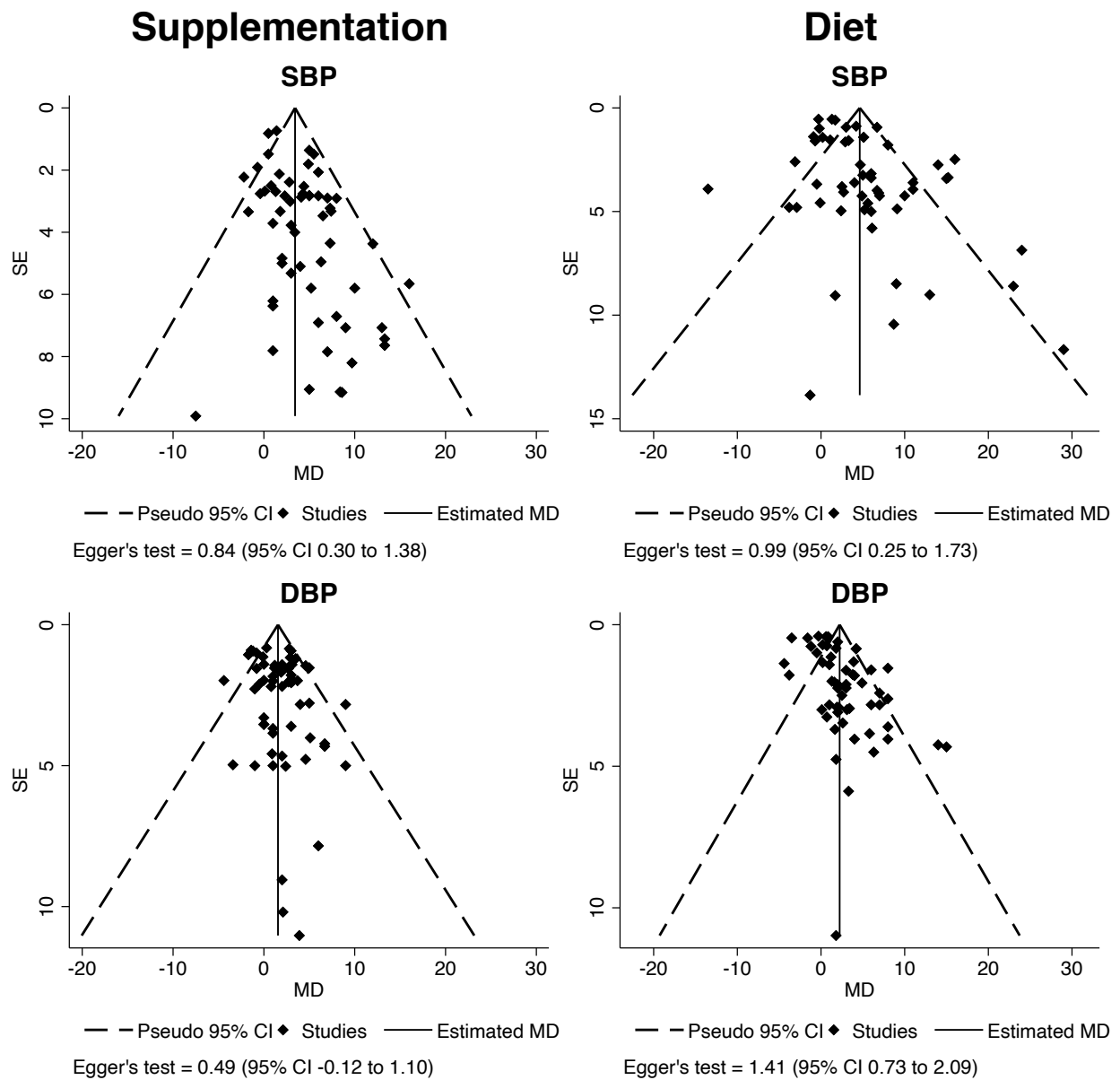


Figure XV. Funnel plots for mean difference (MD) of changes in systolic (SBP) and diastolic (DBP) blood pressure levels (as mmHg) and its standard error (SE) using trim-and-fill methods for small-study effects by type of intervention (supplementation vs diet). Squared-diamonds indicate filled data.

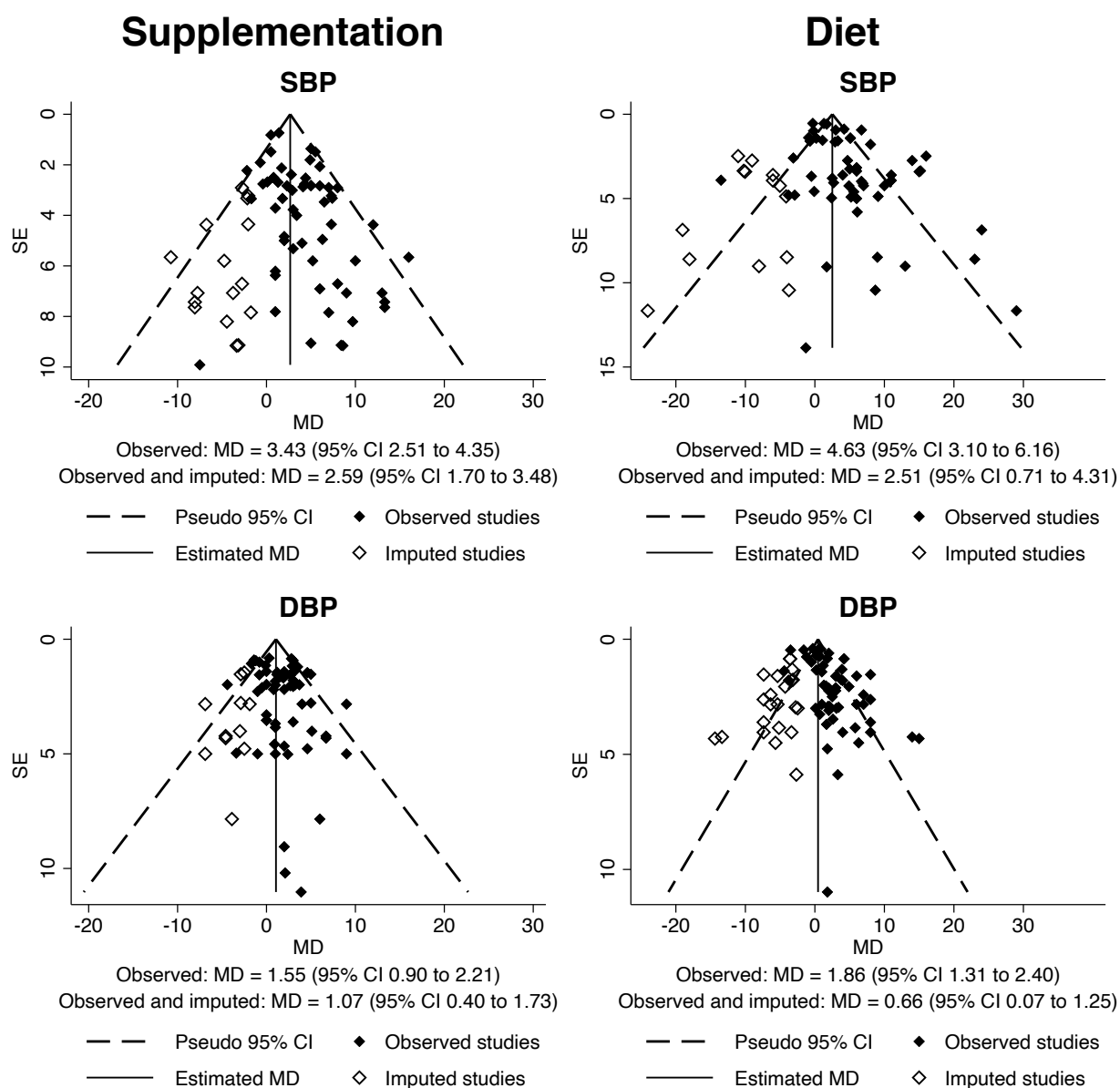


Figure XVI. Funnel plots for mean difference (MD) of changes in systolic (SBP) and diastolic (DBP) blood pressure levels (as mmHg) and its standard error (SE) divided by hypertension status.

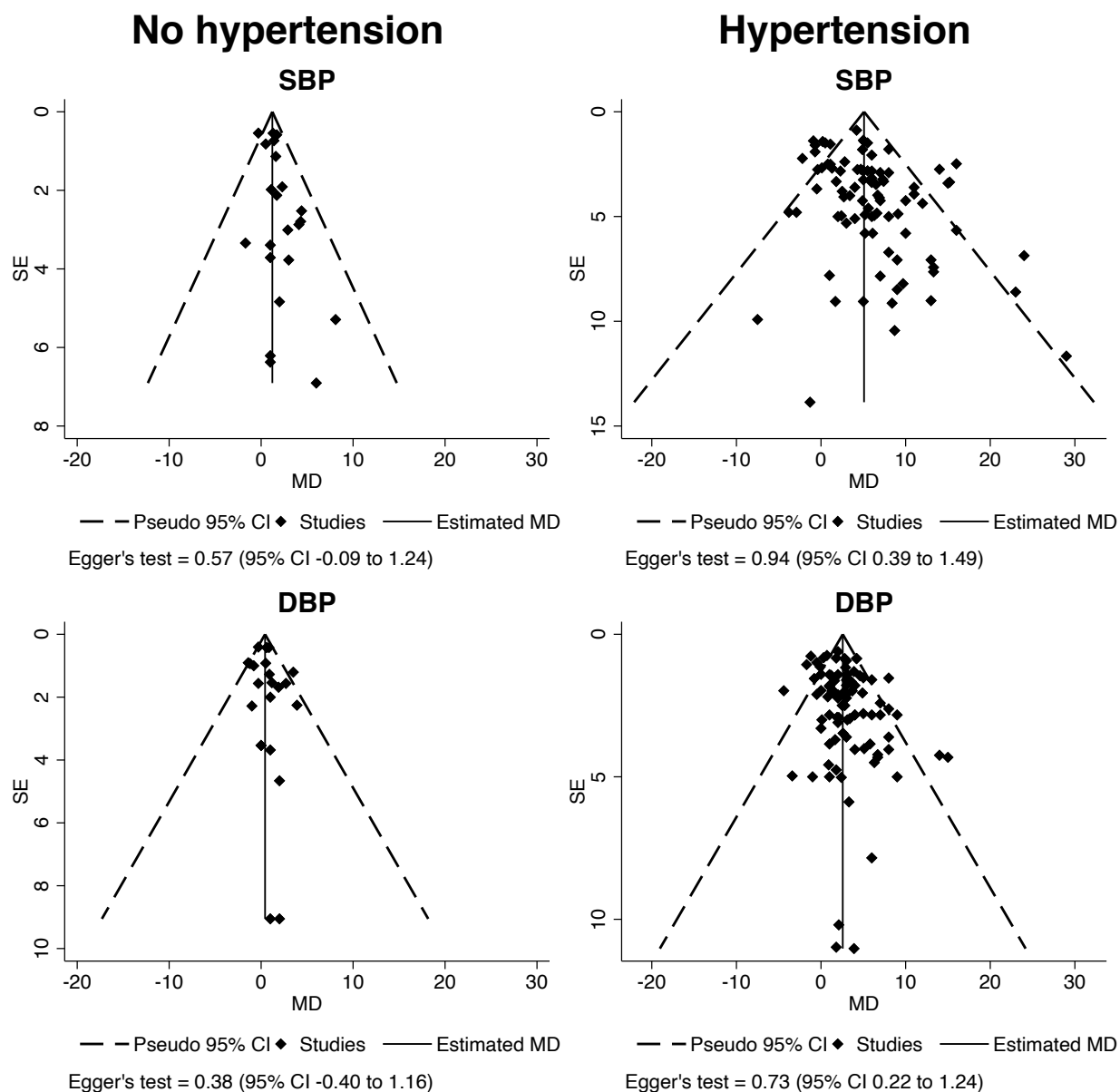


Figure XVII. Funnel plots for mean difference (MD) of changes in systolic (SBP) and diastolic (DBP) blood pressure levels (as mmHg) and its standard error (SE) using trim-and-fill methods for small-study effects divided by hypertension status. Squared-diamonds indicate filled data.

